Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (page i).

In the Claims

Please cancel Claims 16, 17, 21, 22, 25, 26 and 29-40. Claims 1, 4-9, 11-15, 18-20, 23, 24, 27, 28 and 41-45 have been amended and are presented below in amended form, and new Claims 46-56 have been added. In accordance with 37 C.F.R. § 1.121(c)(1)(ii), amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages ii-vii).

1. (Amended Five Times) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin, said immunoglobulin or fragment comprising an antigen-binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin, said antigen-binding region comprising at least one of three complementarity determining regions (CDR1, CDR2 and CDR3) of a light chain variable region and at least one of three complementarity determining regions (CDR1, CDR2 and CDR3) of a heavy chain variable region of the amino acid sequence set forth below such that the antibody specifically binds to the α4β7 integrin:

| | | |
|---|---|---|
| light chain: | CDR1 | amino acids 44-59 of SEQ ID NO: 12 |
| | CDR2 | amino acids 75-81 of SEQ ID NO: 12 |
| | CDR3 | amino acids 114-122 of SEQ ID NO: 12 |
| heavy chain: | CDR1 | amino acids 50-54 of SEQ ID NO: 15 |
| | CDR2 | amino acids 69-85 of SEQ ID NO: 15 |
| | CDR3 | amino acids 118-129 of SEQ ID NO: 15. |

4. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 2 wherein the antigen-binding region is of rodent origin.

5. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 2 comprising:

an immunoglobulin light chain variable region comprising the amino acid sequence of amino acids 21-132 of SEQ ID NO:12; and

an immunoglobulin heavy chain variable region comprising the amino acid sequence of amino acids 20-140 of SEQ ID NO:15.

6. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 1 wherein the portion of an immunoglobulin of human origin is derived from a human framework region.

7. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 6, wherein said immunoglobulin or fragment can compete with Act-1 monoclonal antibody (ATCC Accession No. PTA-3663) for binding to $\alpha 4\beta 7$ integrin.

8. (Amended Five Times) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for $\alpha 4\beta 7$ integrin comprising a heavy chain and a light chain,

the light chain comprising complementarity determining regions derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a light chain variable region of human origin, wherein each of said complementarity determining regions (CDR1, CDR2 and CDR3) comprises the amino acid sequence set forth below:

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12; and

the heavy chain comprising complementarity determining regions derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a heavy chain variable region of human origin, wherein each of said complementarity

determining regions (CDR1, CDR2 and CDR3) comprises the amino acid sequence set forth below:

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

9. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said immunoglobulin can compete with murine Act-1 monoclonal antibody (ATCC Accession No. PTA-3663) for binding to $\alpha 4\beta 7$.

11. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said light chain variable region of human origin is the light chain variable region of the human GM607'CL antibody (SEQ ID NO: 8).

12. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said heavy chain variable region of human origin is the heavy chain variable region of the human 21/28'CL antibody (SEQ ID NO: 10).

13. (Amended Five Times) A humanized immunoglobulin light chain or antigen-binding portion thereof comprising complementarity determining regions (CDR1, CDR2 and CDR3) of the light chain of murine Act-1 antibody (ATCC Accession No. PTA-3663), and a framework region derived from a light chain variable region of human origin, said complementarity determining regions comprising the amino acid sequences set forth below such that an antibody or antigen-binding fragment thereof comprising said light chain or antigen-binding portion thereof specifically binds to the $\alpha 4\beta 7$ integrin:

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12.

14. (Twice Amended) The humanized immunoglobulin light chain or antigen-binding portion thereof of Claim 13 wherein the human framework region is derived from the light chain variable region of the human GM607'CL antibody (SEQ ID NO: 8).

15. (Twice Amended) The humanized immunoglobulin light chain or antigen-binding portion thereof of Claim 14 comprising the variable region of SEQ ID NO:21.

18. (Amended Five Times) A humanized immunoglobulin heavy chain or antigen-binding portion thereof comprising complementarity determining regions (CDR1, CDR2 and CDR3) of the heavy chain of the murine Act-1 antibody (ATCC Accession No. PTA-3663), and a framework region derived from a heavy chain variable region of human origin, said complementarity determining regions comprising the amino acid sequences set forth below such that an antibody or antigen-binding fragment thereof comprising said heavy chain or antigen-binding portion thereof specifically binds to the $\alpha 4\beta 7$ integrin:

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

19. (Twice Amended) The humanized immunoglobulin heavy chain or antigen-binding portion thereof of Claim 18 wherein the human framework region is derived from the heavy chain variable region of the human 21/28'CL antibody (SEQ ID NO: 10).

20. (Twice Amended) The humanized immunoglobulin heavy chain or antigen-binding portion thereof of Claim 19 comprising the variable region of SEQ ID NO:19.

23. (Amended Three Times) A humanized immunoglobulin light chain, the amino acid sequence of said light chain comprising at least an antigen-binding portion of the light chain variable region amino acid sequence shown in Figure 7 (amino acids 21-132 of SEQ ID NO:12).

24. (Twice Amended) The humanized immunoglobulin light chain of Claim 23, wherein said amino acid sequence of said light chain comprises the signal peptide sequence shown in Figure 7 (amino acids 1-20 of SEQ ID NO:12) and at least an antigen-binding portion of the light chain variable region amino acid sequence shown in Figure 7 (amino acids 21-132 of SEQ ID NO:12).

27. (Amended Three Times) A humanized immunoglobulin heavy chain, the amino acid sequence of said heavy chain comprising at least an antigen-binding portion of the heavy chain variable region amino acid sequence shown in Figure 9 (amino acids 20-140 of SEQ ID NO:15).

28. (Twice Amended) The humanized immunoglobulin heavy chain of Claim 27, wherein said amino acid sequence of said heavy chain comprises the signal peptide sequence shown in Figure 9 (amino acids 1-19 of SEQ ID NO:15) and at least an antigen-binding portion of the heavy chain variable region amino acid sequence shown in Figure 9 (amino acids 20-140 of SEQ ID NO:15).

41. (Amended) A method of inhibiting the interaction of a first cell bearing $\alpha 4\beta 7$ with a second cell bearing a ligand thereof, comprising contacting said first cell with an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

42. (Amended) A method of inhibiting leukocyte infiltration of mucosal tissue, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

43. (Amended) A method of therapy of a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

44. (Amended) The method of Claim 43, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM-1.

45. (Amended) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

46. (New) A method of inhibiting the interaction of a first cell bearing $\alpha 4\beta 7$ with a second cell bearing a ligand thereof, comprising contacting said first cell with an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

47. (New) A method of inhibiting leukocyte infiltration of mucosal tissue, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

48. (New) A method of therapy of a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

49. (New) The method of Claim 48, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM-1.

50. (New) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin comprising a heavy chain and a light chain, wherein:

said light chain comprises complementarity determining regions (CDR1, CDR2 and CDR3) derived from an antibody of nonhuman origin which binds α4β7 and a framework region derived from a light chain variable region of human origin, wherein said complementarity determining regions (CDR1, CDR2 and CDR3) comprise the amino acid sequences set forth below:

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12; and

said heavy chain comprises complementarity determining regions (CDR1, CDR2 and CDR3) derived from an antibody of nonhuman origin which binds α4β7 and a framework region derived from a heavy chain variable region of human origin, wherein said complementarity determining regions (CDR1, CDR2 and CDR3) comprise the amino acid sequences set forth below:

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

51. (New) The method of Claim 50 wherein said inflammatory bowel disease is ulcerative colitis.

52. (New) The method of Claim 50 wherein said inflammatory bowel disease is Crohn's disease.

53. (New) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin comprising a heavy chain and a light chain, wherein said heavy chain comprises the variable region of SEQ ID NO:19 and said light chain comprises the variable region of SEQ ID NO:21.

54. (New) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin comprising a heavy chain and a light chain, wherein said heavy chain comprises the variable region of SEQ ID NO:19 and said light chain comprises the variable region of SEQ ID NO:21.

55. (New) The method of Claim 54 wherein said inflammatory bowel disease is ulcerative colitis.

56. (New) The method of Claim 54 wherein said inflammatory bowel disease is Crohn's disease.

## REMARKS

Amendments to the Specification

The Specification has been amended to refer to biological material (murine Act-1 hybridoma cell line which produces the murine Act-1 monoclonal antibody) described in the application as filed and subsequently deposited under the Budapest Treaty at the American Type Culture Collection (ATCC). As required by 37 C.F.R. § 1.809(d), the Specification has been amended to recite: (a) the accession number of the deposit; (b) the date of deposit; and (c) the name and address of the depository. A copy of the ATCC Deposit Receipt and Viability Statement for murine hybridoma Act-1 is provided herewith.

A Statement under 37 C.F.R. § 1.804(b) and a Statement under 37 C.F.R. § 1.806 and § 1.808 are being filed concurrently, completing the formal requirements for the biological deposit.